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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,044	07/13/2005	Andrew David Morley	06275-460US1 100928-1P US	8677
26164 7590 01/14/2008 FISH & RICHARDSON P.C. P.O BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER ANDERSON, REBECCA L	
			ART UNIT 1626	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/542,044

Applicant(s)

MORLEY ET AL.

Examiner

Rebecca L. Anderson

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 08 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-10, 13-15 and 17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-3 and 5-10 is/are allowed.
- 6) ☒ Claim(s) 13-15 and 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1-3, 5-10, 13-15 and 17 are currently pending in the instant application. Claims 1-3 and 5-10 appear allowable and claims 13-15 and 17 are rejected. Claim 13 is also objected.

#### ***Response to Amendment and Arguments***

Applicant's amendment and arguments filed 8 November 2007 have been considered and entered into the application. Applicants' amendment has overcome the objection to the claims as containing non-elected subject matter.

In regards to the 35 USC 112 1<sup>st</sup> paragraph rejection, Applicants' argue that the claims have been narrowed to recite specific disorders that are present in the specification and have been demonstrated to be related to IKK-2. Applicant's arguments filed 8 November 2007 have been fully considered but they are not persuasive. Specifically, while applicant has provided some in vitro assay data for the claimed compounds, this assay data does not support claims to methods of treating and preventing the claimed diseases as receptor activity is generally unpredictable and a highly structure specific area, and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the compounds of the claims and to extrapolate to the in vivo treatment or prevention of the claimed diseases. Therefore, claims 13-15 and 17 are rejected under 35 USC 112 1<sup>st</sup> paragraph.

#### ***Claim Objections***

Claim 13 is objected to because of the following informalities: Specifically, claim 13 reads "A method or the treatment or prophylaxis...(emphasis added)". It is

suggested that the first instance of the term "or" be amended to the word "for".

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-15 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

### The nature of the invention

The nature of the invention of claims 13-5 and 17 is the method of treating or preventing cancer and various inflammatory diseases such as asthma and rheumatoid arthritis. The prophylaxis or "to prevent" actually means to anticipate or counter in advance, to keep from happening etc. and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compositions can be administered to order to have the "prevention" effect.

### The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat or prevent which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art

would recognize that in regards to therapeutic and preventive effects of the above listed diseases, whether or not the disease is effected by IKK-2 would make a difference.

Applicants are claiming methods which include the treatment of various diseases such as cancer and various inflammatory disorders.

Applicants claim a method of treating or reducing the risk of cancer. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

In regards to the treatment of the listed inflammatory disorders, enablement for the scope of treating inflammatory disorders generally is not present. For a compound

or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually in any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. There are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. This discussion, demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to accept any agent to be able to treat inflammation generally.

For example, Rheumatoid arthritis, remains a clinical entity of unknown etiology (Gripenberg, page 85).

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment and prevention by affecting IKK-2 one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims due to the unpredictability of the role of IKK-2 and, for example, since it is known that the etiology of rheumatoid arthritis is unknown.

***The amount of direction or guidance present and the presence or absence of working examples***

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable or preventable by affecting IKK-2 on page 15. In vitro assay data is found on pages 32-36. However, the disclosure does not provide how this in vitro data correlates to the treatment or prevention of the assorted list of disorders of the instant claims. There are no working examples present for the treatment or prevention of any specific disease or disorder. Further, there is no disclosure regarding how all types of the diseases having diverse mechanisms are treated or prevented. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

Applicants have not provided any competent evidence or disclosed tests that are



highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

### The breadth of the claims

The breadth of the claims is the method of treating or preventing various inflammatory diseases and cancer.

### The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited (treated or prevented) by affecting IKK-2 and would furthermore then have to determine which of the claimed compounds would provide treatment or prevention of which disease, if any.

### *The level of the skill in the art*

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the

compound of the instant claims for of treating or preventing the various inflammatory diseases or cancer, as a result necessitating one of skill to perform an exhaustive search for which diseases can be treated or prevented by what compounds of the instant claims in order to practice the claimed invention. (Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated or prevented by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the method claims.

### Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Rebecca Anderson/  
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9 January 2008